Serial No. 10/018,377

Claim Amendments

In accordance with revised 37 C.F.R. 1.121, a listing of all claims that are, or were, in the application is provided below. This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently amended): Ultralente ~~like~~ crystals having a uni-modal particle size distribution comprising:

a) insulin, ~~an insulin analog, a derivatized insulin, or a derivatized insulin analog~~LysB28, ProB29-human insulin, AspB28-human insulin, or acylated insulin; and

b) a divalent metal cation; characterized in that the volume mean spherical equivalent diameter of the crystals is from 1 micron to 5 microns.

2. (Original): Crystals according to Claim 1, wherein the divalent metal cation is zinc.

3. (Currently amended): Crystals according to Claim 2 wherein zinc is present at about 0.3 to about 2.0 mole per mole of insulin, ~~insulin analog, derivatized insulin or derivatized insulin analog~~ LysB28, ProB29-human insulin, AspB28-human insulin, or acylated insulin.

4. (Previously amended): Crystals according to ~~claim~~ Claim 1, wherein the volume mean spherical equivalent diameter is from 1.5 microns to 4.5 microns.

5. (Original): Crystals according to Claim 4 wherein the volume mean spherical equivalent diameter is from 2 microns to 4 microns.

6. (Currently amended): A process for preparing crystals according to Claim 1, comprising;

a) preparing a crystallization solution comprising insulin, ~~an insulin analog, a derivatized insulin, or a derivatized insulin analog~~ LysB28, ProB29-human insulin, AspB28-human insulin, or acylated insulin, a buffer, a salt and a divalent cation;

b) combining the crystallization insulin, ~~an insulin analog, a derivatized insulin, or a derivatized insulin analog~~ LysB28, ProB29-human insulin, AspB28-human insulin, or acylated insulin solution of step a) with a nucleating seed suspension; and

c) allowing time for the seeded crystallization solution of step b) to generate the crystals.

7. (Original): The process of Claim 6 wherein the nucleating seed suspension comprises insulin, ~~or a derivatized insulin~~ LysB28, ProB29-human insulin, AspB28-human insulin, or acylated insulin.

8. (Previously amended): The process of Claim 6 wherein the volume of nucleating seed suspension is ~~equivalent to~~ about 5 to about 20 percent of the volume of the seeded crystallization solution.

9. (Previously amended): The process of Claim 8 wherein the volume of nucleating seed suspension is ~~equivalent to~~ about 8 to about 20 percent of the volume of the seeded crystallization solution.

10. (Previously amended): The process of Claim 9 wherein the volume of nucleating seed suspension is ~~equivalent to~~ about 10 to about 15 percent of the volume of the seeded crystallization solution.

11. (Previously amended): The process of Claim 6 wherein the seeded crystallization solution has a protein concentration between about 0.5 ~~to~~ and about 20 mg/ml.

12. (Previously amended): The process of Claim 11 wherein the seeded crystallization solution has a protein concentration between about 1 ~~to~~ and about 10 mg/ml.

13. (Previously amended): The process of Claim 12 wherein the seeded crystallization solution has a protein concentration ~~of~~ between about 2 ~~to~~ and about 4 mg/ml.

14. (Original): The process of Claim 6 wherein the divalent metal cation is zinc.

15. (Cancelled)

16. (Cancelled)

17. (Cancelled)

18. (Original): The process of Claim 6 wherein the buffer is sodium acetate and the salt is sodium chloride.

19. (Previously amended): The process of Claim ~~8~~ 6 wherein the crystallization solution further comprises citrate.

20. (Previously amended): A pharmaceutical composition ~~for administration by inhalation by mouth~~ comprising the crystals according to ~~claim~~ Claim 1.

21. (Original): The pharmaceutical composition of Claim 20 further comprising a carrier, an additive, an excipient, or an aqueous solvent.

22. (Original): The pharmaceutical composition of Claim 21 wherein the crystals are in the form of a dry powder.

23. (Currently amended): The pharmaceutical composition of Claim 21 further comprising a non-crystalline form of insulin, ~~an insulin analog, a derivatized insulin, or a derivatized insulin analog~~LysB28, ProB29-human insulin, AspB28-human insulin, or acylated insulin.

24. (Cancelled)

25. (Previously amended): A method of using the crystals according to ~~claim~~ Claim 1 to treat diabetes or hyperglycemia using a device to administer the crystals by inhalation via the mouth to a patient in need of such treatment.

26. (Previously amended): A method of treating diabetes comprising administering the pharmaceutical composition according to ~~claim~~ Claim 20 to a patient in need thereof to regulate blood glucose levels in the patient.

27. (Original): The method of treating diabetes according to Claim 26 wherein the pharmaceutical composition is administered once a day to the patient.

28. (Previously added): The crystals of Claim 1, wherein the acylated insulin is a fatty acid-acylated insulin.

29. (Previously added): The process of Claim 6, wherein the acylated insulin is a fatty acid-acylated insulin.

30. (Previously added): The pharmaceutical composition of Claim 20, wherein the crystals comprise a fatty acid-acylated insulin.

31. (Previously added): A method of using the crystals of according to Claim 20 to treat diabetes or hyperglycemia using a device to administer the crystals by inhalation via the mouth to a patient in need of such treatment.

32. (Previously added): A method of treating diabetes comprising administering the pharmaceutical composition according to Claim 30 to a patient in need thereof to regulate blood glucose levels in the patient.